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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1639	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/801,994	JOUNG ET AL.	
	Examiner	Art Unit	
	Mark Shibuya	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *273-300* is/are pending in the application.

4a) Of the above claim(s) *287-292,299 and 300* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *273-286 and 293-298* is/are rejected.

7)☒ Claim(s) *279* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/14/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 273-300 are pending. Claims 287-292, 299 and 300 are withdrawn from consideration. Claims 273-286 and 293-298 are examined.

Election/Restrictions

2. Applicant's election with traverse of Group I, claims 273-298, in the reply, filed on 10/23/2006, is acknowledged. The traversal is on the ground(s) that the asserted materially different process of fusion protein production has not been supported by specific, substantial and credible utilities. Applicant argues that no evidence has been provided "showing that **a** fusion protein could be produced" from the cells of the invention of Group I. Applicant argues that "[i]n the absence of such information, the Restriction cannot be maintained."

This is not found persuasive because restriction does not require evidence for specific, substantial and credible utilities. Applicant does not point to the authority for such a requirement. Furthermore, a population of host cells of the claims of Group I could produce a fusion protein containing an activation tag, wherein the fusion proteins could be used to produce antibody against the said activation tag. The examiner respectfully submits that this constitutes a reason and an example needed to support the restriction requirement.

3. Applicant's election with traverse of the species of a prokaryotic cell, a Gal11P activation tag and a zinc finder polypeptide sequence to be assayed for interaction with a DNA sequence, a His3 reporter gene, in the reply filed on 10/23/2006 is acknowledged. The traversal is on the ground(s) that a search for each allegedly distinct species in no way unduly burdensome. Applicant states that "a search of the art for a host cell comprising a fusion protein including any activation tag and any reporter would necessarily and inevitably reveal art relevant to all allegedly distinct species." Applicant states that is not possible to select a particular and specific transcriptional regulatory sequence and a particular and specific DBD recognition element.

This is not found persuasive because the prior art reference of Dove et al., US 5,925, 523, at col.s 1-3, especially at col. 2, lines 42-65, teach that interaction trap systems, were well-known in the art, and that they differ in the specifics, including DNA binding domains, reporter genes, activation domains. Furthermore, Dove et al., teach eukaryotic and prokaryotic systems. Therefore, the examiner respectfully submits that applicant's argument regarding the necessity and inevitability of the relevant art to disclose all species, is not accurate and not convincing.

In regard to the impossibility of selecting a particular and specific transcriptional regulatory sequence and DBD recognition element, the examiner respectfully finds this statement to be ambiguous and respectfully notes that, for example, the specification states:

> From a structural perspective, DNA-binding proteins containing domains suitable for use as polypeptide components of a composite DNA-binding region may be classified as DNA-binding proteins with a helix-turn-helix structural design, including, but not limited to, MAT 1, MAT 2, MAT a1,

> Antennapedia, Ultrabithorax, Engrailed, Paired, Fushi tarazu, HOX, Unc86, and the previously noted Oct1, Oct2 and Pit; zinc finger proteins, such as Zif268, SWI5, Kruppel and Hunchback; steroid receptors; DNA-binding proteins with the helix-loop-helix structural design, such as Daughterless, Achaete-scute (T3), MyoD, E12 and E47; and other helical motifs like the leucine-zipper, which includes GCN4, C/EBP, c-Fos/c-Jun and JunB. The amino acid sequences of the component DNA-binding domains may be naturally-occurring or non-naturally-occurring (or modified).

Specification at p. 91, lines 7-16. Independent claim 273 is drawn to a transcriptional regulatory sequence comprising one or more DBD elements for a DNA-binding domain. However, solely in reliance upon applicant's assertion in this regard, and in the interest of compact prosecution, the examiner withdraws the species requirement in regard to election of a specific and particular transcriptional regulatory sequence and a particular and specific DBD recognition element.

The requirement is still deemed proper and is therefore made FINAL.

4. Claims 299 and 300 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 287-292 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10/23/2006.

Priority

5. This application, filed 3/16/2004, states that it is a continuation of 09/858,852, filed 5/16/2001, now abandoned, which claims benefit of 60/204,509, filed 5/16/2000.

Information Disclosure Statement

6. The information disclosure statement filed 6/14/2004, fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein, in regard to citations B4-B8 only, have not been considered because no copies of this are found in prior Application Serial No. 09/990,762.

Specification

7. The drawings show nucleotide/amino acid sequences which must be identified by a sequence identifier, either in the drawings themselves, or in the Brief Description of the Drawings, as appropriate. The examiner respectfully requests applicant's help in identifying such sequences.

8. Applicant is respectfully requested to update the priority data found in the first line of the specification, pursuant to 35 USC 120.

Claim Objections

9. Claim 279 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 279 is drawn to an RNA polymerase, an RNA polymerase subunit, etc., but claim 278, from which claim 279 depends, is drawn to RNA polymerase, only.

Claim Rejections - 35 USC § 112, Second Paragraph

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 273-286 and 293-298 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 273, and its dependent claims, are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: the polynucleotide encoding a fusion protein, the transcriptional regulatory sequence, and the reporter gene operably linked to the transcriptional regulatory sequence.

Claim 273 recites the abbreviation "DBD", which renders the claim vague and indefinite, because the abbreviation should be spelled out to make clear what it stands for.

Claim 273 states the language "a DNA-binding domain" in line 7, and "a DNA-binding domain " in line 10, so that it is unclear as to whether the domain in line 10 is the same as the domain in line 7.

Claim 273 recites the limitation "a DBD recognition element", in line 10, respectively. There is uncertain antecedent basis for this limitation in the claim.

Claim 275 recites the language "the desired level of expression", which lack sufficient antecedent basis. Furthermore, "the desired level", appears to read upon a mental process, such that it is unclear how the structure of the reporter gene is further limited, so that one of skill in the art would not be apprised of the metes and bounds of the claimed invention.

Claim 279 recites the limitation "the intermediary peptide" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 273-285 and 293-298 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Dove et al., 5,925,523 A**, (IDS filed 6/14/2004, cite no. A2), and in view of **Jappelli et al.**, Biochem. Biophys. Res. Commun. (1999) Vol. 266, pp. 243-247.

The claims are drawn to a population of host cells, each host cell comprising: (a) a polynucleotide encoding a fusion protein, the fusion protein comprising (i) an activation tag; and (ii) a polypeptide sequence to be assayed for its interaction with a DNA sequence, (b) a transcriptional regulatory sequence comprising one or more binding sites (DBD recognition elements) for a DNA-binding domain; (c) a reporter gene operably linked to the transcriptional regulatory sequence, wherein expression of the reporter gene is modulated when the polypeptide sequence interacts with a DBD recognition element; wherein at least 10^7 unique pairs of a DBD recognition element and a fusion protein are represented in the population of host cells; and variations thereof.

Dove et al., 5,925,523 A, throughout the patent, and e.g., at col. 26, lines 60-67, line 65-col. 4, line 24, disclose expressing peptide libraries intracellulary, and Dove et al., at claims 35 and 36, claim providing a population of prokaryotic host cells comprising a chimeric gene which encodes a fusion protein, the fusion protein including a test polypeptide and an activation tag, and a reporter gene operably linked to a transcriptional regulatory sequence which includes a binding site (DBD recognition element) for a DNA-binding domain, wherein interaction of the test polypeptide of the fusion protein with the DBD recognition element in the host cells results in a measurable change in expression of the reporter gene; which reads upon a population of host cells, each host cell comprising: (a) a polynucleotide encoding a fusion protein, the fusion protein comprising (i) an activation tag; and (ii) a polypeptide sequence to be assayed for its interaction with a DNA sequence, (b) a transcriptional regulatory sequence comprising one or more binding sites (DBD recognition elements) for a DNA-binding domain; (c) a reporter gene operably linked to the transcriptional regulatory sequence, wherein expression of the reporter gene is modulated when the polypeptide sequence interacts with a DBD recognition element.

Dove et al., states:

> The present invention makes available an interaction trap system (hereinafter "ITS") which is derived using recombinantly engineered prokaryotic cells. As described in the appended examples, the prokaryotic ITS derives in part from the unexpected finding that the natural interaction between a transcriptional activator and subunit(s) of an RNA polymerase complex can be replaced by heterologous protein-protein interactions which are capable of activating transcription. The versatility of the prokaryotic ITS makes it generally suitable for many, if not all of the applications of the eukaryotic ITS. Moreover, the ease of manipulation of the bacterial cells, e.g., in transformation or transfection and culturing,

> means that even larger polypeptide libraries can be screened in the prokaryotic ITS.

Dove et al., at col. 6, lines 40-54. Thus Dove et al., teach an interaction trap system used in recombinant prokaryotic cells, (as in instant claim 274), wherein the engineered cells are used to express polypeptide libraries for screening for interaction that activates transcription.

Dove et al., at col. 2, line 66-col. 3, line 10, teach reporter genes that confer a growth advantage, and as in instant claims 275 and 283-285.

Dove et al., at col. 9, line 61-col. 10, line 5, teaches that activation tags can interact directly or indirectly with polymerase complexes. Dove et al., state:

> The term "activation tag" refers to a polypeptide sequence which participates as a component of an RNA polymerase, or which recruits an active polymerase complex. For instance, in the prokaryotic ITS the activation tag can be a polymerase interaction domain or some other polypeptide sequence which interacts with, or is covalently bound to, one or more subunits (or a fragment thereof) of an RNA polymerase complex. Activation tags can also be sequences which are derived from, e.g., transcription factors or other proteins which interact with, directly or indirectly, wit polymerase complexes. Activation tags can even be from random polypeptide libraries.

Dove et al., at col. 9, line 61-col. 10, line 5. Furthermore, Dove et al., state:

> By "covalently bonded" it is meant that two domains are joined by covalent bonds, directly or indirectly. That is, the "covalently bonded" proteins or protein moieties may be immediately contiguous or may be separated by stretches of one or more amino acids within the same fusion protein.

Dove et al., at col. 10, lines 61-65. Thus Dove et al., teach and suggest activation tags that interact indirectly with RNA polymerase via an intermediary polypeptide, wherein the said polypeptide is covalently fused to an RNA polymerase, as in claims 278 and 279.

Dove et al., at e.g., col. 5, lines 41-50, and Figure 2, teach an activation tag of Gal11P and Gal4, as in claims 280 and 281. Dove et al., e.g., at col. 8, lines 14-34, teach vector constructs, as in claim 282.

Dove et al., at col. 12, lines 21-30, teach DBD recognition elements that are zinc fingers/zinc clusters, as in claims 295 and 298.

Dove et al., do not disclose at least 10^7 unique pairs of a DBD recognition element and a fusion protein in a population of host cells, as in claims 273, and 293-298.

Jappelli et al., Biochem. Biophys. Res. Commun. (1999) Vol. 266, pp. 243-247, throughout the publication, and especially at the abstract, p. 243, para 5-p. 247, para 1; Tables 1 and 2, teach methods of identifying dimerizing polypeptides using a homodimerization system in *E. coli*, where fusion proteins libraries comprising a plurality of sequences encoding random test polypeptides were selected for the capacity to dimerize in a bacteriophage λ repressor dimerization assay, and wherein the library comprises 10^{10} members, as evidenced by ten-fold dilutions of 10^{-10} pfu/ml phage stock that produced a visible lysis of the bacterial lawn.

It would have been *prima facie* obvious at the time the invention was made for one of ordinary skill in the art to have made and used a population of host cells, each host cell comprising at least 10^{10} unique pairs of a DBD recognition element and a fusion protein are represented in the population of host cells; including libraries that contain polypeptide DBD recognition elements, and libraries that contain polypeptide sequences, as in instant claims 293-298.

One of ordinary skill in the art would have been motivated to have made and used a population of host cells, each host cell comprising at least 10^7 unique pairs of a DBD recognition element and a fusion protein are represented in the population of host cells, because Jappelli et al. at p. 247, para 1, state: "Regardless of the specific mechanism of interaction, the identification of novel sequences promoting protein oligomerization may be important to understand the evolution of natural protein structures. In addition, it may be interesting for protein engineering applications." Also, Dove et al., at col. 6, lines 40-54, teach using transfected host cells to screen polypeptide libraries, as part of an interaction trap system.

One of ordinary skill in the art would have had a reasonable expectation of success in making and using a population of host cells, each host cell comprising at least 10^7 unique pairs of a DBD recognition element and a fusion protein are represented in the population of host cells, because Jappelli et al. used such libraries to identify dimerizing polypeptides in homodimerization bacterial systems and because Dove et al., teach a population of host cells containing polypeptide libraries, and teach as part of an interaction trap system.

14. Claim 286 is rejected under 35 U.S.C. 103(a) as being unpatentable over **Dove et al., 5,925,523 A**, (IDS filed 6/14/2004, cite no. A2), and in view of **Jappelli et al.**, Biochem. Biophys. Res. Commun. (1999) Vol. 266, pp. 243-247, as applied to claims 273-285, 293-298, above, and further in view of **Sadowski et al., US 5885779 A**.

Claim 286 is drawn to a population of host cells, wherein the growth advantage of the host cells is controllable by varying the concentration of 3-aminotriazole.

The references of **Dove et al., 5,925,523 A**, (IDS filed 6/14/2004, cite no. A2), and **Jappelli et al.**, are relied upon, as set forth, *supra*.

Dove et al., and Jappelli et al., do not disclose varying the concentration of 3-aminotriazole to control the growth advantage of the host cells.

Sadowski et al., US 5885779 A, state:

> An additional modification of the RTA assay of the invention may be useful to discriminate between strong and weak inhibitors of bait and prey interaction. The histidine analog 3-aminotriazole (3-AT) is a competitive inhibitor of the HIS3 gene product. 3-AT added to the growth medium to cause a requirement for stronger expression of the HIS3 gene in order to overcome the 3-AT inhibitory effect. In certain embodiments, the level of HIS3 expression required for growth in the absence of histidine may be directly proportional to the concentration of 3-AT in the growth medium (23). The results of such an assay may be evaluated on the premise that stronger inhibitors of a specific interaction between the bait and prey fusion proteins should allow cell growth on higher concentrations of 3-AT.

Sadowski et al., US 5885779 A, col. 20, lines 19-34. Claim 286

It would have been *prima facie* obvious, at the time the invention was made, for one of ordinary skill in the art to have made and used a population of host cells, wherein the growth advantage of the host cells is controllable by varying the concentration of 3-aminotriazole.

One of ordinary skill in the art would have been motivated to make and use a population of host cells, wherein the growth advantage of the host cells is controllable by varying the concentration of 3-aminotriazole, in order to discriminate between strong and weak interaction in the interaction trap assay.

One of ordinary skill in the art would have had a reasonable expectation of success in using 3-aminotriazole, because its use in growth assays of bait and prey systems was known in prior art.

Double Patenting

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. Claims 273-275, 282, 293, 294, 296, 297 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over **claims 35 and 36 of U.S. Patent No. 5925523 A**, in view of **Jappelli et al.**, Biochem. Biophys. Res. Commun. (1999) Vol. 266, pp. 243-247.

The claims are drawn to a population of host cells, each host cell comprising: (a) a polynucleotide encoding a fusion protein, the fusion protein comprising (i) an activation tag; and (ii) a polypeptide sequence to be assayed for its interaction with a DNA sequence, (b) a transcriptional regulatory sequence comprising one or more binding sites (DBD recognition elements) for a DNA-binding domain; (c) a reporter gene operably linked to the transcriptional regulatory sequence, wherein expression of the reporter gene is modulated when the polypeptide sequence interacts with a DBD recognition element; wherein at least 10^7 unique pairs of a DBD recognition element and a fusion protein are represented in the population of host cells; and variations thereof.

Dove et al., 5,925,523 A, throughout the patent, and e.g., at col. 26, lines 60-67, line 65-col. 4, line 24, disclose expressing peptide libraries intracellulary, and Dove et al., at claims 35 and 36, claim methods comprising providing a population of prokaryotic host cells comprising a chimeric gene which encodes a fusion protein, the fusion protein including a test polypeptide and an activation tag, and a reporter gene operably linked to a transcriptional regulatory sequence which includes a binding site (DBD recognition element) for a DNA-binding domain, wherein interaction of the test polypeptide of the fusion protein with the DBD recognition element in the host cells results in a measurable change in expression of the reporter gene; which reads upon a population of host cells, each host cell comprising: (a) a polynucleotide encoding a fusion protein, the fusion protein comprising (i) an activation tag; and (ii) a polypeptide sequence to be assayed for its interaction with a DNA sequence, (b) a transcriptional regulatory sequence

comprising one or more binding sites (DBD recognition elements) for a DNA-binding domain; (c) a reporter gene operably linked to the transcriptional regulatory sequence, wherein expression of the reporter gene is modulated when the polypeptide sequence interacts with a DBD recognition element, as in the instant claims.

Dove et al., do not disclose at least 10^7 unique pairs of a DBD recognition element and a fusion protein in a population of host cells, as in claims 273-275, 282, 293, 294, 296, 297.

Jappelli et al., Biochem. Biophys. Res. Commun. (1999) Vol. 266, pp. 243-247, throughout the publication, and especially at the abstract, p. 243, para 5-p. 247, para 1, Tables 1 and 2, teach methods of identifying dimerizing polypeptides using a homodimerization system in *E. coli*, where fusion proteins libraries comprising a plurality of sequences encoding random test polypeptides were selected for the capacity to dimerize in a bacteriophage λ repressor dimerization assay, and wherein the library comprises 10^{10} members, as evidenced by ten-fold dilutions of 10^{-10} pfu/ml phage stock that produced a visible lysis of the bacterial lawn.

It would have been *prima facie* obvious at the time the invention was made for one of ordinary skill in the art to have made and used a population of host cells, each host cell comprising at least 10^{10} unique pairs of a DBD recognition element and a fusion protein are represented in the population of host cells; including libraries that contain polypeptide DBD recognition elements, and libraries that contain polypeptide sequences, as in instant claims 273-275, 282, 293, 294, 396, 297.

One of ordinary skill in the art would have been motivated to have made and used a population of host cells, each host cell comprising at least 10^7 unique pairs of a DBD recognition element and a fusion protein are represented in the population of host cells, because Jappelli et al. at p. 247, para 1, state: "Regardless of the specific mechanism of interaction, the identification of novel sequences promoting protein oligomerization may be important to understand the evolution of natural protein structures. In addition, it may be interesting for protein engineering applications." Also, Dove et al., at col. 6, lines 40-54, teach using transfected host cells to screen polypeptide libraries, as part of an interaction trap system.

One of ordinary skill in the art would have had a reasonable expectation of success in making and using a population of host cells, each host cell comprising at least 10^7 unique pairs of a DBD recognition element and a fusion protein are represented in the population of host cells, because Jappelli et al. used such libraries to identify dimerizing polypeptides in homodimerization bacterial systems and because Dove et al., teach a population of host cells containing polypeptide libraries, and teach as part of an interaction trap system.

17. Claims 273-275, 282, 293-298 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over **claims 1-5 of copending Application No. 10/915,233**, in view of **Jappelli et al.**, Biochem. Biophys. Res. Commun. (1999) Vol. 266, pp. 243-247.

Claims 1-5 of copending **Application No. 10/915,233**, are drawn to a method for detecting an interaction between a test polypeptide and a DNA sequence, comprising: i providing a population of host cells wherein each cell contains (a) a first reporter gene operably linked to a transcriptional regulatory sequence which includes one or more binding sites (DBD recognition elements) for a DNA-binding domain, (b) a second reporter gene operably linked to a transcriptional regulatory sequence which includes one or more binding sites (DBD recognition elements) for a DNA-binding domain, (c) a chimeric gene which encodes a fusion protein, the fusion protein including a test polypeptide, a weak DNA-binding domain and an activation tag, wherein binding of the weak DNA-binding domain of (c) to the binding sites of (a) or (b) does not cause a significant increase in the expression of the first reporter gene or the second reporter gene; wherein expression of the first reporter gene results in a first detectable signal; wherein expression of the second reporter gene results in a second detectable signal; wherein a non-specific interaction between a test polypeptide of the fusion protein and a DBD recognition element of the first and second reporter genes results in an increased level of expression of the first and second reporter genes; wherein a specific interaction between a test polypeptide of the fusion protein and a DBD recognition element of the first or second reporter gene results in a desired level of expression of either the first or second reporter gene; and ii isolating host cells comprising a fusion protein that specifically interacts with a DBD recognition element of the first or second reporter gene exhibiting a desired level of expression of the first or second reporter gene, thereby detecting an interaction between the test polypeptide and a DBD recognition element

DNA sequence; and wherein the DNA-binding domain comprises zinc fingers. Thus the claims of the co-pending application are narrower in scope than the claims of the instant invention.

Claims 1-5 of copending Application No. 10/915,233, do not disclose at least 10^7 unique pairs of a DBD recognition element and a fusion protein in a population of host cells, as in claims 273-275, 282, 293, 294, 396, 297.

Jappelli et al., Biochem. Biophys. Res. Commun. (1999) Vol. 266, pp. 243-247, throughout the publication, and especially at the abstract, p. 243, para 5-p. 247, para 1, Tables 1 and 2, teach methods of identifying dimerizing polypeptides using a homodimerization system in *E. coli*, where fusion proteins libraries comprising a plurality of sequences encoding random test polypeptides were selected for the capacity to dimerize in a bacteriophage λ repressor dimerization assay, and wherein the library comprises 10^{10} members, as evidenced by ten-fold dilutions of 10^{-10} pfu/ml phage stock that produced a visible lysis of the bacterial lawn.

It would have been *prima facie* obvious at the time the invention was made for one of ordinary skill in the art to have made and used a population of host cells, each host cell comprising at least 10^{10} unique pairs of a DBD recognition element and a fusion protein are represented in the population of host cells; including libraries that contain polypeptide DBD recognition elements, and libraries that contain polypeptide sequences, as in instant claims 273-275, 282, 293-298.

One of ordinary skill in the art would have been motivated to have made and used a population of host cells, each host cell comprising at least 10^7 unique pairs of a

DBD recognition element and a fusion protein are represented in the population of host cells, because Jappelli et al. at p. 247, para 1, state: "Regardless of the specific mechanism of interaction, the identification of novel sequences promoting protein oligomerization may be important to understand the evolution of natural protein structures. In addition, it may be interesting for protein engineering applications."

One of ordinary skill in the art would have had a reasonable expectation of success in making and using a population of host cells, each host cell comprising at least 10^7 unique pairs of a DBD recognition element and a fusion protein are represented in the population of host cells, because Jappelli et al. used such libraries to identify dimerizing polypeptides in homodimerization bacterial systems.

This is a provisional obviousness-type double patenting rejection.

Conclusion

18. Claims 273-286 and 293-298 are rejected.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Shibuya whose telephone number is (571) 272-0806. The examiner can normally be reached on M-F, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. James Schultz can be reached on (571) 272-0763. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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